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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

Date: 15-AUG-2007

Subject: PP# 6E7150. Etoxazole. Registration for Use on Cherries, Hops, and Melon Subgroup 9A. Summary of Analytical Chemistry and Residue Data.

DP#:	335334	Decision#: 330258
PC Code:	107091	MRID#: 470036-01 thru 470036-03
40 CFR:	180.593	Chemical Class: unclassified acaricide

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Executive Summary

Etoxazole [2-(2,6-difluorophenyl)-4-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydrooxazole] is a contact acaricide/ovicide that is currently registered in the United States (U.S.) for the control of mites on various raw agricultural commodities (RACs). Permanent tolerances have been established for residues of etoxazole in/on plant commodities, ranging from 0.05 ppm for cottonseed to 1.0 ppm for cotton gin byproducts [40 CFR §180.593(a)]. Tolerances have also been established for etoxazole residues in fat (0.02 ppm) and liver (0.01 ppm) of ruminants and in milk fat (0.01 ppm).

The Interregional Research Project Number 4 (IR-4) has submitted a petition (PP# 6E7150) proposing uses for etoxazole, formulated as Zeal® Wettable Powder (WP; EPA Reg. No. 59639-123) and Secure® WP (EPA Reg. No. 59639-138) on cherries, hops, and melon subgroup 9A. The petitioner has proposed the establishment of permanent tolerances for etoxazole residues of 0.70 ppm in/on cherries; 7.0 ppm in/on hop, dried cones; and 1.5 ppm in/on melon, subgroup 9A.

Received in
RRC 8/21/2007
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The qualitative nature of etoxazole residues in plants is understood based upon the plant metabolism studies on cotton, eggplant, apple and orange. In plants, etoxazole may undergo photo-oxidation to yield Metabolite R-13. Parent and Metabolite R-13 then undergo opening of the oxazole ring to form a variety of metabolites (R-4, R-7, R-14, and R-3), and subsequent cleavage of the opened ring forms Metabolites DFB, R-8, R-10, R-11, R-12, and R-15.The HED Metabolism Assessment Review Committee (MARC, 4/23/03) concluded that only parent should be included in the tolerance expression for all plant commodities. For risk assessment purposes, only parent will be considered for most plant commodities; however, Metabolite R-3 should also be included in the risk assessment for cotton gin byproducts and almond hulls.

In the crop field trials submitted with the current petition, residues of etoxazole were determined using modifications of previously submitted gas chromatography (GC) with nitrogen-phosphorus detector (NPD) or mass-selective detector (MSD) methods (Methods RM-37, or RM-37HM). These methods have been reviewed by HED and deemed adequate for data collection. The methods and any modifications were also adequately validated in conjunction with the sample analyses. In addition, the current tolerance enforcement methods are adequate for enforcing the proposed tolerances on the proposed tolerances. The aforementioned methods were forwarded to the Analytical Chemistry Laboratory (ACL) for Agency petition method validations (PMVs) (Memos, J. Tyler, 6/17/03; D290912 and D290914).

Food and Drug Administration (FDA) multiresidue methods (MRMs) may be used to determine residues of etoxazole in fatty and non-fatty matrices and to determine residues of Metabolite R-3 in nonfatty matrices. Etoxazole was completely recovered from fortified samples of apple using Methods 302, E1 with GC/NPD or Method 303, C1 or C2 with GC/NPD. Etoxazole was partially recovered from cottonseeds (fatty matrix) using Method 304, E5, C1 or C2 with GC/NPD. Metabolite R-3 could be completely recovered from cotton gin byproducts using Method 302, E4 using GC/NPD. However, matrix interferences enhanced the recoveries of R-3 from gin byproducts. The results of the MRM testing were forwarded to the FDA for inclusion in the Pesticide Analytical Method (PAM) Vol. I (Memo, J. Tyler, 6/17/03; D290919).

Adequate storage stability data are available to support the current magnitude of the residue and processing studies. The available hop storage stability data are adequate to support crop field trial data. For cherries and cantaloupe, adequate storage stability data are available; however, residue values were corrected in order to correct for storage dissipation (64% and 67% for cherries and cantaloupe, respectively).

The submitted cherry field trial data reflect a total of 2 foliar applications of etoxazole (Zeal® 72 WDG) on tart and sweet cherries at a rate of 0.135 pounds (lb) active ingredient (ai)/acre (A)/application for a total application rate of 0.27 lb ai/A [2x the maximum proposed seasonal application rate; preharvest interval (PHI)=7 days]. The results show that corrected residues of etoxazole (corrected for storage dissipation) in tart and sweet pitted cherries were 0.31-1.2 ppm and 0.13-0.28 ppm, respectively.

The submitted cantaloupe field trial data reflect a total of 2 foliar applications of etoxazole (Zeal® 72 WDG) on cantaloupes at a rate of 0.135 lb ai/A/application for a total application rate of 0.27 lb ai/A (2x the maximum proposed seasonal application rate; PHI=5-8 days). The results show

that residues of etoxazole (corrected for storage dissipation) in cantaloupe were 0.016-0.12 ppm.

The submitted hop field trial data reflect a total of 2 foliar applications of etoxazole (Zeal® 72 WDG) on hops at a rate of 0.198 lb ai/A, for at total application rate of approximately 0.396 lb ai/A (~3x the maximum proposed seasonal application rate; PHI=6-7 days). The results show that residues of etoxazole in dried hop cones were 1.98-4.18 ppm.

The application rates used in the cherry (2 applications at 0.135 lb ai/A/application for a total application rate of 0.27 lb ai/A), cantaloupe (2 applications at 0.135 lb ai/A/application for a total application rate of 0.27 lb ai/A), and hop field trials (2 applications at 0.198 lb ai/A/application for a total application rate of 0.396 lb ai/A) do not match the proposed application rates (1 application at 0.135 lb ai/A for cherry and melon; 1 application at 0.180 lb ai/A for hops). However, as the residue decline data show that residues decrease in cherries and cantaloupe with increasing PHIs, the majority of the residues seen the field trials would most likely be due to the second application. Therefore, potential residues of etoxazole in/on cherries and cantaloupe will not be underestimated. Based on the highest-average field trial (HAFT) residues in cherries and cantaloupe the residue data are adequate to support tolerances for cherry, tart (0.60 ppm); cherry, sweet (0.20 ppm); and vegetable, cucurbit subgroup 9A (0.15 ppm). For hops, the available residue decline data show that residues of etoxazole do not decrease significantly in dried hop cones with increasing PHIs. Based on the HAFT residue of 4.14 ppm, the available data are adequate to support a conditional registration and a permanent tolerance of 5.0 ppm on hop, dried cones. The registration should be made unconditional upon submission of additional side-by-side data as follows: 1 trial each at 2 x 0.198 = 0.396 lb ai/A (exaggerated application rate, PHI = 7 days) and one at 0.180 lb ai/A (proposed application rate, PHI = 7 days), 4 samples per trial. As R3 is a metabolite of concern in cotton gin byproducts, and a metabolism data are not available for hops, R3 is a potential residue of concern for this crop. Therefore, the requested side-by-side hop field trial should include data for R3, as well as the parent. Subsequent to the submission of these data, RAB1 will make a determination as to whether or not R3 is a residue of concern in hops.

There are no rotational crop restrictions on the proposed labels. HED concluded that, based on the available confined rotational crop data, no rotational crop restrictions would be required for rotational crops following applications at rates totaling 0.135 lb ai/A/season, which is the maximum proposed application rate for cantaloupe (the only proposed use that is considered to be a rotated crop). Therefore, the available rotational crop data are adequate to support the proposed uses.

There are no established or proposed Codex, Canadian or Mexican maximum residue limits (MRLs) for etoxazole; therefore, harmonization is not an issue for this action.

Residue Chemistry Deficiencies

- Revised Section F.
- Additional residue data on hops as follows: 1 trial each at 2 x 0.198 = 0.396 lb ai/A (exaggerated application rate, PHI = 7 days) and one at 0.180 lb ai/A (proposed application rate, PHI = 7 days), 4 samples per trial. As R3 is a metabolite of concern in cotton gin byproducts, and a metabolism data are not available for hops, R3 is a potential residue of concern for this crop. Therefore, the requested side-by-side hop field trial should include data for R3, as well as the parent. Subsequent to the submission of these data, RAB1 will make a determination as to whether or not R3 is a residue of concern in hops.

Recommendations

Provided a revised Section F is submitted and successful Agency PMVs of the analytical enforcement methods are reported, the available residue chemistry data support the establishment of the following:

- Unconditional registration and permanent tolerances for residues of etoxazole *per se* in/on the following RACs: cherry, sweet (0.60 ppm); cherry, tart (0.20 ppm); and vegetable, cucurbit subgroup 9A (0.15 ppm).
- Conditional registration and permanent tolerance for residues of etoxazole *per se* in/on hop, dried, cone at 5.0 ppm. The registration should be made unconditional upon submission of additional residue data as specified above.

A human-health risk assessment is forthcoming.

Background

Etoxazole is a contact acaricide/ovicide used for the control of tetranychid mite species. It is currently registered for use on cotton, pome fruits, and strawberries. Permanent tolerances have been established for residues of etoxazole in/on plant commodities, ranging from 0.05 ppm in cottonseed to 1.0 ppm in cotton gin byproducts [40 CFR §180.593(a)]. Tolerances have also been established for etoxazole residues in fat (0.02 ppm) and liver (0.01 ppm) of ruminants and in milk fat (0.01 ppm).

IR-4 has submitted a petition (PP# 6E7150) proposing uses for etoxazole, formulated as Zeal™ WP Miticide and Secure™ Miticide , in the U.S. on cherries, hops, and melon subgroup 9A. In conjunction with these uses, the petitioner has proposing the establishment of permanent tolerances for etoxazole residues in/on the following plant RACs: cherry at 0.70 ppm; hop, dried cones at 7.0 ppm; and melon, subgroup 9A at 0.15 ppm. The nomenclature and physicochemical properties of etoxazole are presented below in Tables 1 and 2.

Table 1. Nomenclature of Etoxazole

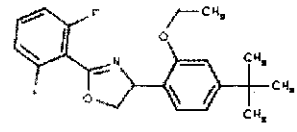
Compound	
Common name	Etoxazole
Company experimental names	S-1283, V-1283, YI-5301
IUPAC name	(*RS*)-5-*tert*-butyl-2-[2-(2,6-difluorophenyl)-4,5-dihydro-1,3-oxazol-4-yl]phenetole
CAS name	2-(2,6-difluorophenyl)-4-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydrooxazole
CAS #	153233-91-1
End-use products/EP	72% WDG (Zeal® WP Miticide and Secure™ Miticide)

Table 2. Physicochemical Properties of Etoxazole (TGAI)

Parameter	Value		References
Melting range	101.5-102.5°C		46018505.der.wpd
pH	6.2		
Density	1.2389 g/cm^3		
Water solubility	3.99 x 10^{-5} at 10°C 7.04 x 10^{-5} at 20°C 6.69 x 10^{-5} at 30°C		
Solvent solubility (g/L at 20°C)	acetone: 309 ethyl acetate: 249 methanol: 104	1,2-dichloroethane: 402 n-heptane: 18.7 xylene: 252	
Vapor pressure at 25°C	7.0 x 10^{-6} pascals		
Dissociation constant (pK_a)	no measurable pK_a		
Octanol/water partition coefficient Log(K_{OW})	5.52 ± 0.58 at 20°C		
UV/visible absorption	Not available.		

860.1200 Directions for Use

Table 3. Summary of Proposed Directions for Use of Etoxazole.

Application, Timing, Type, and Equipment	Formulation (EPA Reg. No.)	Application Rate (lb ai/A)		Maximum Number Applications/ Season	RTI (days) [1]	PHI (days) [1]	Use Directions and Limitations [2]
		Per App.	Per Season				
Cherry (Sweet and Tart)							
Broadcast foliar application; ground equipment.	Secure™ Miticide (59639-123)	0.09-0.135	0.135	1	-	7	A minimum application volume of 50 gallon/A is recommended.
	Zeal® WP Miticide (59639-138)	0.09-0.135	0.135	1	-	7	A minimum application volume of 50 gallon/A is recommended.
Hops							
Broadcast foliar application; ground equipment.	Secure™ Miticide (59639-123)	0.135-0.18	0.18	1	-	7	A minimum application volume of 50 gallon/A is recommended.
	Zeal® WP Miticide (59639-138)	0.135-0.18	0.18	1	-	7	A minimum application volume of 50 gallon/A is recommended.
Melon Subgroup 9A							
Broadcast foliar application; ground equipment.	Secure™ Miticide (59639-123)	0.09-0.135	0.135	1	-	7	A minimum application volume of 50 gallon/A is recommended.
	Zeal® WP Miticide (59639-138)	0.09-0.135	0.135	1	-	7	A minimum application volume of 50 gallon/A is recommended.

1. RTI = minimum retreatment interval; PHI = minimum preharvest interval.
2. The proposed label does not include any rotational crop restrictions.

HED Conclusions. Although the submitted cherry, cantaloupe, and hop crop field trials were conducted at exaggerated rates (~2-3x), HED concludes that the data are adequate to support the proposed uses. However, the registration on hops should be conditional until additional crop field trial data are submitted.

860.1300 Nature of the Residue - Plants

The qualitative nature of etoxazole residues in plants is understood based upon the plant metabolism studies on cotton, eggplant, apple and orange. In each of the studies, the major ^{14}C-residue in/on various matrices was identified as parent compound. Based on the metabolite profiles observed in these studies, etoxazole may undergo photo-oxidation to yield Metabolite R-13. Parent and Metabolite R-13 then undergo opening of the oxazole ring to form a variety of metabolites (R-4, R-7, R-14, and R-3), and subsequent cleavage of the opened ring forms Metabolites DFB, R-8, R-10, R-11, R-12, and R-15.

Based on the above studies, the MARC (Memo, J. Tyler, 6/17/03; D289666) concluded that parent is the only residue of concern in plant commodities for purposes of the tolerance expression and risk assessment. However, for cotton gin byproducts, the risk assessment should also include Metabolite R-3. In addition, based on the results of the crop field trial on almonds,

HED has determined that Metabolite R-3 should also be included in the risk assessment for almond hulls (Memo, J. Tyler, 3/30/05; D303628).

860.1340 Residue Analytical Methods

Adequate methods are available for enforcing the current plant and livestock tolerances. In the current trials and processing study, samples were analyzed using either the proposed enforcement methods or a slightly modified version of current enforcement methods.

The GC/MSD method used to analyze etoxazole residues in/on cherry samples in the crop field trial study is a slightly modified version of a previously-validated method (Method RM-37HM). The method was adequately validated in conjunction with the sample analyses. The validated LOQ was 0.0037 ppm and the LOD was 0.0012 ppm for etoxazole in/on cherries.

The GC/NPD methods used to analyze etoxazole residues in/on cantaloupe fruit and dried hop cones in the respective crop field trials are slightly modified version of a previously-validated method (Method RM-37). The method was adequately validated in conjunction with the sample analyses. The validated LOQs were 0.0046 ppm and 0.2 ppm for cantaloupe and hops, respectively; and the validated LODs were 0.0015 ppm and 0.1 ppm for etoxazole in/on cantaloupe and hops, respectively.

HED Conclusions. The GC/NPD or MSD methods used in the submitted field trials are adequate for determining residues of etoxazole in cherries, cantaloupe, and hops. The current tolerance enforcement methods are also adequate for enforcing the proposed tolerances given the similarity between these commodities and the plant commodities with established tolerances (cottonseed, apple, strawberry, and tangerine). The aforementioned methods were forwarded to the ACL for Agency PMVs (Memos, J. Tyler, 6/17/03; D290912 and D290914).

860.1360 MRM

FDA MRMs may be used to determine residues of etoxazole in fatty and non-fatty matrices and to determine residues of Metabolite R-3 in nonfatty matrices. Etoxazole was completely recovered from fortified samples of apple using Methods 302, E1 with GC/NPD or Method 303, C1 or C2 with GC/NPD. Etoxazole was partially recovered from cottonseeds (fatty matrix) using Method 304, E5, C1 or C2 with GC/NPD. Metabolite R-3 could be completely recovered from cotton gin byproducts using Method 302, E4 using GC/NPD. However, matrix interferences enhanced the recoveries of R-3 from gin byproducts. The results of the MRM testing were forwarded to the FDA for inclusion in the PAM Vol. I (Memo, J. Tyler, 6/17/03; D290919).

860.1380 Storage Stability

The maximum storage intervals for treated samples in the cherry, cantaloupe, and hop crop field trial studies were 179, 72, and 60 days, respectively. Previously-submitted storage stability data

(Memo, J. Tyler, 7/17/03; D283737) indicate that etoxazole is stable at -20°C for at least 3.5 months in apples, 2 months in strawberries, 6 months in orange pulp, 12 months in orange peels, 17 months in cottonseed, and 6 months in cotton gin byproducts. Additional storage stability data conducted in conjunction with the current cherry, cantaloupe, and hop field trials were submitted. In the cherry crop field trial study, samples fortified with 0.10 ppm and analyzed a 193 days had an average recovery of 64%. In the cantaloupe crop field trial study, samples fortified with 0.10 ppm and analyzed at 50 and 126 days had average corrected recoveries of 64% and 70%, respectively. In the hops crop field trial study, samples fortified with 0.10 ppm and analyzed at 84 days had an average corrected recovery of 101%.

HED Conclusions: The available hop storage stability data are adequate to support crop field trial data. For cherries and cantaloupe, adequate storage stability data are available; however, residue values were corrected in order to correct for storage dissipation (64% and 67% for cherries and cantaloupe, respectively).

860.1480 Meat, Milk, Poultry, and Eggs

There are no livestock feed commodities associated with the proposed uses.

860.1500 Crop Field Trials

47003601.der (cherries)
47003602.der (cantaloupe)
47003603.der (hops)

IR-4 has submitted cherry, cantaloupe and hop field trial data supporting the proposed uses of etoxazole. The results from the currently reviewed field trials are discussed below and summarized in Table 4.

Table 4. Summary of Residues from the Crop Field Trials with Etoxazole.

Crop Matrix	Application Rate (lb ai/A) *[g ai/A]*	PHI (days)[1]	Etoxazole Residues (ppm)[2]					
			N	Min	Max.	HAFT[3]	Mean	Std. Dev.
Cherries (proposed use = 0.135 lb ai/A total application rate, 7-day PHI)								
Tart Cherry[4]	0.271-0.297	6-8	14	0.31	1.2	0.88	0.48	0.23
Sweet Cherry[4]	0.272-0.2897	6-8	12	0.13	0.28	0.29	0.20	0.050
Melon Subgroup 9A (proposed use = 0.135 lb ai/A total application rate, 7-day PHI)								
Cantaloupe fruit[4]	0.264-0.278	5-8	18	0.016	0.12	0.12	0.042	0.027
Hops (proposed use = 0.18 lb ai/A total application rate, 7-day PHI)								
Dried hop cones	0.3620.396 *[165.7-181.4]*	6-7	6	1.98	4.18	3.96	3.45	0.96

1. PHI = preharvest interval.
2. The LOQs are 0.0037 ppm, 0.0046 ppm, and 0.2 ppm in/on cherries, cantaloupe and hops, respectively; the LOD was 0.0012 ppm, 0.0015 ppm, 0.1 ppm on cherries, cantaloupe, and hops, respectively.
3. HAFT = highest-average field trial.
4. Corrected residue values to account for storage dissipation were used to determine residue summary information.

Cherries: IR-4 has submitted field trial data for etoxazole on cherries. A total of thirteen (seven with tart cherries and six with sweet cherries) were conducted in the United States during the 2004 growing season encompassing Regions 1 (NJ, n=1 tart), 5 (MI, n=6 – 4 tart and 2 sweet), 9 (CO, n=1 tart), 10 (CA, n=2 sweet), 11 (WA and ID, n=2 – 1 tart and 1 sweet), and 12 (OR, n=1 sweet).

At each trial location, a total of 2 foliar-directed applications of Zeal® 72 WDG, a water-dispersible granule formulation containing 72% etoxazole as the ai, were applied at a rate of approximately 0.135 lb ai/A/application (1x the maximum proposed single application rate) at 12- to 14-day retreatment intervals (RTIs) for a total application rate of approximately 0.27 lb ai/A (2x the maximum proposed seasonal application rate). Samples were harvested 6-8 days following the second application. Additional samples were collected at the 04-WA13 and 04-MI16 at approximately 3, 7, and 14 days after the final application in order to determine residue decline. No spray additives were added to the spray mixture.

Residues of etoxazole were 0.20-0.76 ppm in/on 14 tart cherry samples, and 0.082-0.18 ppm in/on 12 sweet cherry samples harvested 6-8 days following two foliar applications of etoxazole totaling ~0.27 lb ai/A. The results show that corrected residues of etoxazole (corrected for storage dissipation) in tart and sweet pitted cherries were 0.31-1.2 ppm and 0.13-0.28 ppm, respectively. The highest-average field trial (HAFT) residues of etoxazole in tart and sweet cherries were 0.56 ppm and 0.17 ppm, respectively. The results of the decline trials indicate that residues of etoxazole declined to a maximum of 0.25 ppm by 14 days in tart cherries, and 0.096 ppm in sweet cherries.

Melon Subgroup 9A: IR-4 has submitted field trial data for etoxazole on cantaloupe. A total of nine field trials were conducted in the United States during the 2004 growing season encompassing Regions 2 (MD and GA, n=2), 5 (WI, n=1), 6 (TX, n=2), and 10 (NM and CA, n=4).

At each trial location, a total of 2 broadcast foliar applications of Zeal® 72 WDG, a water-dispersible granule formulation containing 72% etoxazole as the ai, were applied at a rate of approximately 0.135 lb ai/A/application (1x the maximum proposed single application rate) at 21-day RTIs for a total application rate of approximately 0.27 lb ai/A (2x the maximum proposed seasonal application rate). Samples were harvested 5-8 days following the second application. Additional samples were collected at the 04-NM01 at approximately 3, 8, and 14 days after the final application in order to determine residue decline. No spray additives were added to the spray mixture.

Residues of etoxazole were 0.016-0.12 ppm in/on 18 cantaloupe samples harvested 5-8 days following two foliar applications of etoxazole totaling ~0.27 lb ai/A. The results show that residues of etoxazole (corrected for storage dissipation) in cantaloupe were 0.016-0.12 ppm. The HAFT was 0.12 ppm. The results of the decline trial indicate that residues of etoxazole declined to a maximum of 0.010 ppm by 14 days.

Hops: IR-4 has submitted field trial data for etoxazole on hops. A total of three field trials were conducted in the United States during the 2003 growing season encompassing Regions11 (WA and ID, n=2), and 12 (OR, n=1).

At each trial location, a total of 2 foliar airblast applications of Zeal™ 72 WDG, a water-dispersible granule formulation containing 72% etoxazole as ai, were applied at a rate of approximately 0.198 lb ai/A [90.7 grams (g) ai/A/application; ~1x the maximum proposed single application rate], for at total application rate of approximately 0.396 lb ai/A (181.4 g ai/A; ~2x the maximum proposed seasonal application rate). For one trial, a second plot was treated with 2 foliar airblast applications at 0.396 lb ai/A/application (181.4 g ai/A/application), for a total application rate of 0.792 lb ai/A (362.8 g ai/A). All applications were made at 14- to 15-day RTIs, and hop cones were harvested at commercial maturity, at 6- to 7-day PHIs. Additional hop samples were harvested at 2-, 6-, 13-, and 20-day PHIs from one trial site to examine residue decline. All samples were dried in commercial driers after harvest. A single control and duplicate treated samples were collected from each trial.

Residues of etoxazole were 1.98-4.18 ppm in/on 6 dried hop cone samples harvested 6-7 days following two foliar applications of etoxazole totaling ~0.396 lb ai/A. The results show that residues of etoxazole in dried hop cones were 1.98-4.18 ppm. The HAFT residue of etoxazole in dried hop cones was 4.14 ppm. Residue decline data show that residues of etoxazole do not decrease significantly in dried hop cones with increasing PHIs.

HED Conclusions. For cherries, the crop field trial data are classified as acceptable and satisfy the guideline requirement for crop field trials (Residue Chemistry Guidelines OPPTS 860.1500). The location and distribution of the field trials differ slightly from the recommended distribution and locations. A total of thirteen (seven with tart cherries and six with sweet cherries) were conducted in Regions 1 (NJ, n=1 tart), 5 (MI, n=6 – 4 tart and 2 sweet), 9 (CO, n=1 tart), 10 (CA, n=2 sweet), 11 (WA and ID, n=2 – 1 tart and 1 sweet), and 12 (OR, n=1 sweet). HED guidelines recommend Regions 1 (NJ, n=1 tart), 5 (MI, n=6 – 4 tart and 2 sweet), 9 (CO, n=1 tart), 10 (CA, n=2 sweet), and 11 (WA and ID, n=2 sweet). However, the available data are adequate to support the proposed use.

The submitted cherry field trial data reflect a total of 2 foliar applications of etoxazole (Zeal® 72 WDG) on tart and sweet cherries at a rate of 0.135 lb ai/A/application for a total application rate of 0.27 lb ai/A (2x the maximum proposed seasonal application rate; PHI=7 days). The results show that corrected residues of etoxazole (corrected for storage dissipation) in tart and sweet pitted cherries were 0.31-1.2 ppm and 0.13-0.28 ppm, respectively. The results of the decline trials indicate that residues of etoxazole declined to a maximum of 0.25 ppm by 14 days in tart cherries, and 0.096 ppm in sweet cherries. The application rates used in the field trials (2 applications at 0.135 lb ai/A/application for a total application rate of 0.27 lb ai/A) does not match the proposed application rate (1 application at 0.135 lb ai/A). As the residue decline data show that residues decrease in cherries with increasing PHIs, the majority of the residues seen the field trials would most likely be due to the second application. Therefore, potential residues of etoxazole in/on cherries will not be underestimated. Based on the HAFT residues of 0.56 ppm and 0.17 ppm in tart and sweet cherries, respectively, the residue data are adequate to support

tolerances of 0.60 ppm and 0.20 ppm for residues of etoxazole on cherry, tart and cherry, sweet.

For cantaloupe, the crop field trial data for cantaloupe are classified as acceptable and satisfy the guideline requirement for crop field trials (Residue Chemistry Guidelines OPPTS 860.1500). The submitted cantaloupe field trial data reflect a total of 2 foliar applications of etoxazole (Zeal® 72 WDG) on cantaloupes at a rate of 0.135 lb ai/A/application for a total application rate of 0.27 lb ai/A (2x the maximum proposed seasonal application rate; PHI=5-8 days). The results show that residues of etoxazole (corrected for storage dissipation) in cantaloupe were 0.016-0.12 ppm. The application rate used in the field trials (2 applications at 0.135 lb ai/A/application for a total application rate of 0.27 lb ai/A) does not match the proposed application rate (1 application at 0.135 lb ai/A). As the residue decline data show that residues decrease in cantaloupe with increasing PHIs, the majority of the residues seen the field trials would most likely be due to the second application. Therefore, potential residues of etoxazole in/on the cucurbit crop subgroup will not be underestimated. Based on the HAFT residue of 0.12 ppm, the residue data are adequate to support a tolerance of 0.15 ppm on vegetable, cucurbit subgroup 9A.

The crop field trial data for hops are classified as acceptable and satisfy the guideline requirement for crop field trials (Residue Chemistry Guidelines OPPTS 860.1500). The submitted hop field trial data reflect a total of 2 foliar applications of etoxazole (Zeal® 72 WDG) on hops at a rate of 0.198 lb ai/A, for at total application rate of approximately 0.396 lb ai/A (~3x the maximum proposed seasonal application rate; PHI=6-7 days). The results show that residues of etoxazole in dried hop cones were 1.98-4.18 ppm. The application rate used in the field trials (2 applications at 0.198 lb ai/A/application for a total application rate of 0.396 lb ai/A) does not match the proposed application rate (1 application at 0.180 lb ai/A). The available residue decline data show that residues of etoxazole do not decrease significantly in dried hop cones with increasing PHIs. Based on the HAFT residue of 4.14 ppm, the available data are adequate to support a conditional registration and a tolerance of 5.0 ppm on hop, dried cones. The registration should be made unconditional upon submission of additional side-by-side residue data as follows: 1 trial each at 2 x 0.198 = 0.396 lb ai/A (exaggerated application rate, PHI = 7 days) and one at 0.180 lb ai/A (proposed application rate, PHI = 7 days), 4 samples per trial. As R3 is a metabolite of concern in cotton gin byproducts, and a metabolism data are not available for hops, R3 is a potential residue of concern for this crop. Therefore, the requested side-by-side hop field trial should include data for R3, as well as the parent. Subsequent to the submission of these data, RAB1 will make a determination as to whether or not R3 is a residue of concern in hops.

860.1520 Processed Food and Feed

As there are no processed commodities associated with the proposed uses, processing studies are not required to support the subject petition.

860.1850/1900 Confined and Field Accumulation in Rotational Crops

Cantaloupes are the only rotated commodity associated with the proposed uses. The results of a confined rotational crop study was submitted and reviewed by HED (Memo, J. Tyler, 7/31/03; D283737). HED made the following recommendation:

> The submitted confined rotational crop study adequately depicts the potential for accumulation of inadvertent etoxazole residues in rotational crops following applications at rates totaling 0.1 lb ai/A/season. As TRR levels were <0.01 ppm in all rotational crop commodities harvested from the ~30-day PBI, no rotational crop restrictions would be required for rotational crops following applications at rates totaling 0.1 lb ai/A/season.

In a separate memo dated 4/6/05, HED made the following recommendation (Memo, J. Tyler; D307178):

> As mentioned above, the submitted confined rotational crop study (45621724.der.wpd) adequately depicts the potential for accumulation of inadvertent etoxazole residues in rotational crops following applications at rates totaling 0.1 lb ai/A/season. In that study, the total radioactive residue (TRR) levels were <0.005 ppm in all rotational crop commodities harvested from the ~30-day plantback interval (PBI).
>
> The newly proposed application rate for strawberries (0.135 lb ai/A) is slightly higher than the rate used in the confined rotational crop study (0.1 lb ai/A). However, all residues were <0.005 ppm in all rotational commodities harvested from the 30-PBI following the 0.1 lb ai/A application. HED does not anticipate a significant increase in inadvertent residues of etoxazole in crops when rotated with strawberries treated with etoxazole at a seasonal rate of 0.135 lb ai/A. The current confined rotational crop study will support the strawberry use; therefore, a new confined rotational crop study is no longer warranted. This deficiency has been resolved.

HED Conclusions: There are no rotational crop restrictions on the proposed labels. HED concluded that, based on the available confined rotational crop data, no rotational crop restrictions would be required for rotational crops following applications at rates totaling 0.135 lb ai/A/season, which is the maximum proposed application rate for cantaloupe. Therefore, the available rotational crop data are adequate to support the proposed uses.

860.1550 Proposed Tolerances

A summary of the recommended tolerances and the correct commodity definitions for the proposed uses are listed in Table 5. As the application rates used in the submitted crop field trials were 2-3x the proposed application rates, the appropriate tolerance levels were determined based on the respective HAFTs. Provided revised Section F is submitted as specified, the residue chemistry database supports the establishment of permanent tolerances for residues of etoxazole in/on the RACs listed in Table 5.

Table 5. Tolerance Summary for Etoxazole

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments (*Correct commodity definition*)
Cherry	0.70	0.60	*Cherry, sweet*
		0.20	*Cherry, tart*
Hop, dried cones	7.0	5.0	
Melon subgroup 9A	0.15	0.15	*Vegetable, cucurbit subgroup 9A*

International Tolerances

There are no established or proposed Codex, Canadian or Mexican MRLs for etoxazole; therefore, harmonization is not an issue for this action [see attached International Residue Limit Status (IRLS) Sheet].

References

DP Barcode: D290919
Subject: PP#2F6420. Multiresidue Method (MRM) Testing of Etoxazole.
From: J. Tyler
To: C. Stafford
Dated: 6/17/2003
MRID(s): 45621825

DP Barcode: D289666
Subject: Etoxazole: Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Decision Document.
From: J. Tyler
To: Y. Donovan
Dated: 6/17/2003
MRID(s): None

DP Barcode: D283737
Subject: PP's# 2F6420. Etoxazole. Registration for Use on Cotton, Pome fruits, Strawberries and Imported Oranges. Summary of Analytical Chemistry and Residue Data.
From: J. Tyler
To: S. Nguyen/D. Kenny
Dated: 7/31/2003
MRID(s): 45621724, 45621725, and 45621801 through 45621825

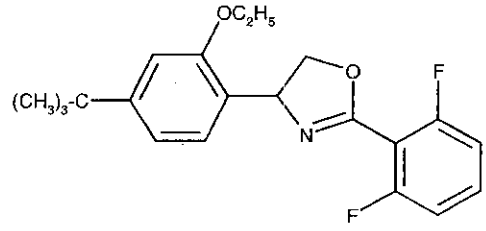
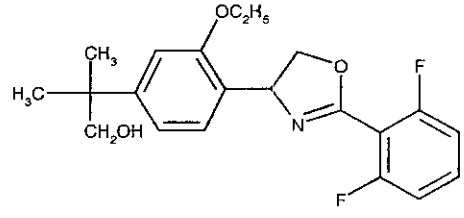
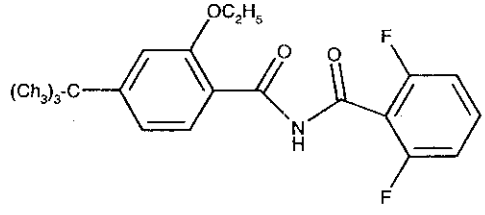
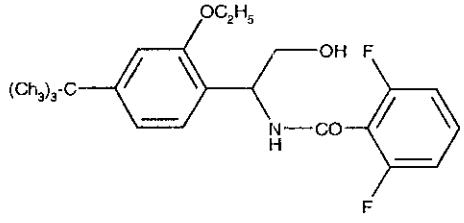
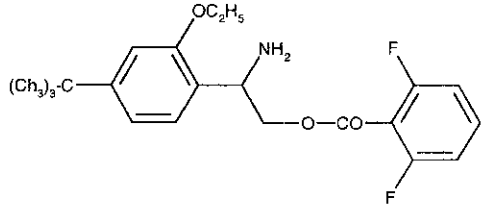
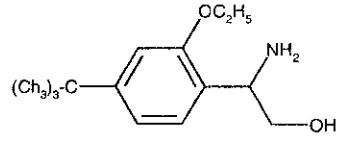
Attachments

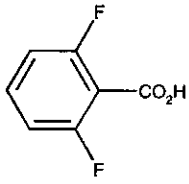
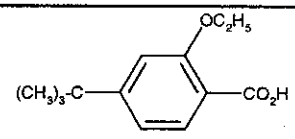
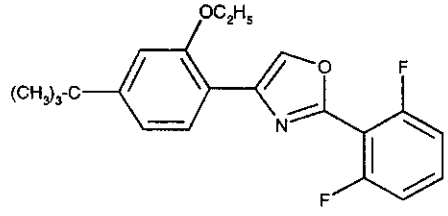
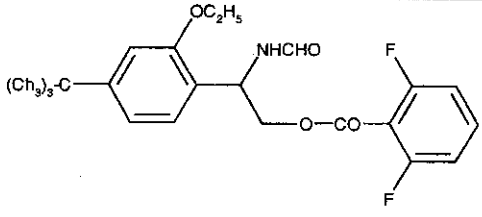
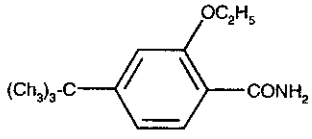
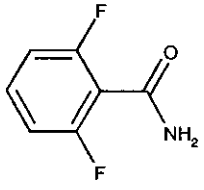
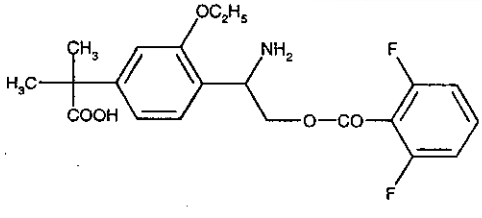
Attachment 1. Structure and Nomenclature.
Attachment 2: IRLS Sheet.

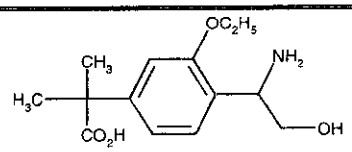
Template Version November 2003

cc (w Attachments): J. Tyler, S. Levy
RDI: RAB1 Chemists (8/01/07); G. Kramer (8/15/07)
J.Tyler:809B:PY:(703)305-5564: 7509P:RAB1

Attachment 1. Structure and Nomenclature.

Common name/(code)	Chemical name	Chemical structure
Etoxazole	2-(2,6-difluorophenyl)-4-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydrooxazole	
R-2	2-(2,6-difluorophenyl)-4-[2-ethoxy-4-(1-hydroxymethyl-1-methylethyl)phenyl]-4,5-dihydrooxazole	
R-3	*N*-(2,6-difluorobenzoyl)-4-*tert*-butyl-2-ethoxybenzamide	
R-4	*N*-(2,6-difluorobenzoyl)-2-amino-2-(4-*tert*-butyl-2-ethoxyphenyl) ethanol	
R-7	2-amino-2-(4-*tert*-butyl-2-ethoxyphenyl)ethyl-2,6-difluorobenozate	
R-8	2-amino-2-(4-*tert*-butyl-2-ethoxyphenyl) ethanol	

Common name/(code)	Chemical name	Chemical structure
R-11	2,6-difluorobenzoic acid	
R-12	4-*tert*-butyl-2-ethoxybenzoic acid	
R-13	4-(4-*tert*-butyl-2-ethoxyphenyl)-2-(2,6-difluorophenyl)oxazole	
R-14	*N*-formyl-2-amino-2-(4-*tert*-butyl-2-ethoxyphenyl)ethyl 2,6-difluorobenzoate	
R-15	4-*tert*-butyl-2-ethoxybenzamide	
DFB	2,6-difluorobenzamide	
R-7-CO_2H	not provided	

Common name/(code)	Chemical name	Chemical structure
Metabolite 1 R-8-CO_2H tBUr5	2-amino-2-(2-ethoxy-4-(1□-hydroxycarbonyl-1□-methylethyl)phenyl) ethanol	

Attachment 2. IRLS Sheet.

INTERNATIONAL RESIDUE LIMIT STATUS			
Chemical Name: **2-(2,6-difluorophenyl)-4-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydrooxazole**	Common Name: **Etoxazole**	**x Proposed tolerance** Reevaluated tolerance Other	Date: **3/1/07**

Codex Status (Maximum Residue Limits)	U. S. Tolerances
√ No Codex proposal step 6 or above No Codex proposal step 6 or above for the crops requested	Petition Number: **6E7150** DP#s: **335334** Other Identifier:
Residue definition (step 8/CXL): N/A	Reviewer/Branch: **J. Tyler/RAB1**
	Residue definition: **etoxazole *per se***

Crop (s)	MRL (mg/kg)	Crop(s)	Tolerance (ppm)
		Cherry	0.70
		Melon subgroup 9A	0.15
		Hop, dried cone	7.0

Limits for Canada	Limits for Mexico
√No Limits No Limits for the crops requested	No Limits √No Limits for the crops requested
Residue definition: N/A	Residue definition: etoxazole

Crop(s)	MRL (mg/kg)	Crop(s)	MRL (mg/kg)

Notes/Special Instructions:S.funk, 03/05/2007.

Etoxazole/107091/IR-4/959857
DACO 7.4.1/7.4.2/OPPTS 860.1500/OECD IIA 6.3.1, 6.3.2, 6.3.3 and IIIA 8.3.1, 8.3.2, 8.3.3 Crop Field Trial/ Residue Decline - Cherry

Primary Evaluator _____ Date: 15-AUG-2007
Jennifer R. Tyler, Chemist
Registration Action Branch (RAB1)
Health Effect Division (HED; 7509P)

Approved by _____ Date: 15-AUG-2007
George F. Kramer, Ph.D., Senior Chemist
RAB1/HED (7509P)

STUDY REPORTS:

MRID No. 47003601 R. Leonard (10/20/06) Etoxazole: Magnitude of the Residue on Cherry: Lab Identification Number: 09044.04-CAR11. Study No.: IR-4 PR No. 09044. Unpublished study prepared by IR-4 Western Region Laboratory. 182 pages.

EXECUTIVE SUMMARY:

The Interregional Research Project Number 4 (IR-4) has submitted field trial data for etoxazole on cherries. A total of thirteen (seven with tart cherries and six with sweet cherries) were conducted in the United States during the 2004 growing season encompassing Regions 1 (NJ, n=1), 5 (MI, n=6), 9 (CO, n=1), 10 (CA, n=2), 11 (WA and ID, n=2), and 12 (OR, n=1).

At each trial location, a total of 2 foliar-directed applications of Zeal® 72 WDG, a water-dispersible granule formulation containing 72% etoxazole as the active ingredient (ai), were applied at a rate of approximately 0.135 pounds (lb) ai/acre (A)/application at 12- to 14-day retreatment intervals (RTIs) for a total application rate of approximately 0.27 lb ai/A. Samples were harvested 6-8 days following the second application. Additional samples were collected at the 04-WA13 and 04-MI16 at approximately 3, 7, and 14 days after the final application in order to determine residue decline. No spray additives were added to the spray mixture.

The gas chromatography/mass-selective detector (GC/MSD) method used to determine etoxazole residues in/on cherry matrices is a slightly modified version of a previously-validated method (Method RM-37HM). The method was adequately validated in conjunction with the sample analyses. The validated limit of quantitation (LOQ) was 0.0037 ppm and the limit of detection (LOD) was 0.0012 ppm for etoxazole in/on cherries. The maximum frozen storage interval of samples, from harvest to analysis, was 179 days. In a concurrent storage stability study, cherry samples fortified with 0.10 ppm and analyzed a 193 days had an average recovery of 64%. Adequate storage stability data are available; however, residue values were corrected in order to correct for storage dissipation

Residues of etoxazole were 0.20-0.76 ppm in/on 14 tart cherry samples, and 0.082-0.18 ppm in/on 12 sweet cherry samples harvested 6-8 days following two foliar applications of etoxazole totaling ~0.27 lb ai/A. The highest-average field trial (HAFT) residues of etoxazole in tart and

sweet cherries were 0.56 ppm and 0.17 ppm, respectively. Residue decline data show that residues of etoxazole decrease in tart and sweet cherries with increasing pre-harvest intervals (PHIs).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document [DP# D334335].

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. There were minor deviations from regulatory requirements; however, none had a negative impact on the validity of the study.

A. BACKGROUND INFORMATION

Etoxazole is a contact acaricide/ovicide primarily used for the control of tetranychid mite species.

TABLE A.1. Test Compound Nomenclature.

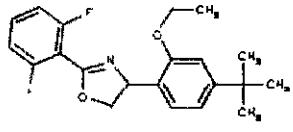
Compound	Chemical Structure
	
Common name	Etoxazole
Company experimental name	S-1283
IUPAC name	(*RS*)-5-*tert*-butyl-2-[2-(2,6-difluorophenyl)-4,5-dihydro-1,3-oxazol-4-yl]phenetole
CAS name	2-(2,6-difluorophenyl)-4-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydrooxazole
CAS #	153233-91-1
End-use product/(EP)	ZEAL® 72 WDG

TABLE A.2. Physicochemical Properties.			
Parameter	Value		References
Melting point/range	101.5-102.5°C		46018505.der.wpd
pH	6.2		
Density	1.2389 g/cm^3		
Water solubility	3.99 x 10^{-5} at 10°C 7.04 x 10^{-5} at 20°C 6.69 x 10^{-5} at 30°C		
Solvent solubility (g/L at 20°C)	acetone: 309 ethyl acetate: 249 methanol: 104	1,2-dichloroethane: 402 n-heptane: 18.7 xylene: 252	
Vapor pressure at 25°C	7.0 x 10^{-6} pascals		
Dissociation constant (pK_a)	No measurable pK_a		
Octanol/water partition coefficient Log(K_{OW})	5.52 ± 0.58 at 20°C		
UV/visible absorption	No ionization at acid or basic pH		

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

TABLE B.1.1 Trial Site Conditions.				
Trial Identification (City, State/Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/g)
09044.04-NJ25 (Bridgeton, NJ/2004)	Sandy loam	2.6	6.4	4.2
09044.04-MI13 (Fennville, MI/2004)	Loamy sand	1.3	4.9	No data
09044.04-MI14 (Fennville, MI/2004)	Sandy loam	3.1	4.8	No data
09044.04-MI15 (Fennville, MI/2004)	Sandy loam	2.6	4.7	No data
09044.04-MI16 (Fennville, MI/2004)	Sandy loam	2.3	4.9	No data
09044.04-CO11 (Hotchkiss, CO/2004)	Clay loam	2.9	7.6	No data
09044.04-ID08 (Buhl, ID/2004)	Silt loam	2.2	8.0	No data
09044.04-MI11 (Fennville, MI/2004)	Sandy clay loam	3.1	5.1	No data
09044.04-MI12 (Fennville, MI/2004)	Sandy clay loam	3.0	5.3	No data
09044.04-OR16 (Hood River, OR/2004)	Sandy loam	4.0	6.5	No data
09044.04-WA13 (Prosser, WA/2004)	Silt loam	1.0	7.2	10.0
09044.04-CA112 (Madera, CA/2004)	Fine sandy loam	0.72	7.7	No data
09044.04-CA113 (Visalia, CA/2004)	Sandy loam	No data	No data	No data

[1] %OM = percent organic matter; CEC = cation-exchange capacity.

Normal weather conditions were reported at all trial sites, with the exception of 04-CA112 and 04-NJ25. At the 04-CA112 trial, it was reported that March was warmer than normal and that April was dryer than normal. At the 04-NJ25 trial, it was reported that precipitation and temperature were above normal during April and that the air temperature was above normal during May. The study reported noted no unusual conditions that would affect the integrity of the study. Rainfall was supplemented with irrigation as needed.

TABLE B.1.2. Study Use Pattern.

Location (City, State/Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants
		Method/Timing	Volume[2]	Rate (lb a.i./A)	RTI[3] (days)	Total Rate (lb a.i./A)	
09044.04-NJ25 (Bridgeton, NJ/2004)	Zeal® 72WDG	1. Foliar directed air blast/fruiting	96	0.135	-	0.272	None
		2. Foliar directed air blast/fruiting	101	0.137	12		
09044.04-MI13 (Fennville, MI/2004)	Zeal® 72WDG	1. Foliar directed air blast/fruiting	102	0.137	-	0.272	None
		2. Foliar directed air blast/fruiting	100	0.135	14		
09044.04-MI14 (Fennville, MI/2004)	Zeal® 72WDG	1. Foliar directed air blast/fruiting	104	0.141	-	0.279	None
		2. Foliar directed air blast/fruiting	102	0.138	14		
09044.04-MI15 (Fennville, MI/2004)	Zeal® 72WDG	1. Foliar directed air blast/fruiting	103	0.139	-	0.275	None
		2. Foliar directed air blast/mature fruit	102	0.137	14		
09044.04-MI16 (Fennville, MI/2004)	Zeal® 72WDG	1. Foliar directed air blast/fruiting	101	0.137	-	0.274	None
		2. Foliar directed air blast/fruiting	101	0.137	14		
09044.04-CO11 (Hotchkiss, CO/2004)	Zeal® 72WDG	1. Foliar directed air blast/fruiting	123	0.142	-	0.277	None
		2. Foliar directed air blast/fruiting – red in color	117	0.135	14		
09044.04-ID08 (Buhl, ID/2004)	Zeal® 72WDG	1. Foliar directed air blast/maturing fruit	100	0.135	-	0.271	None
		2. Foliar directed air blast/maturing fruit	100	0.136	13		
09044.04-MI11 (Fennville, MI/2004)	Zeal® 72WDG	1. Foliar directed air blast/fruiting	101	0.136	-	0.273	None
		2. Foliar directed air blast/fruiting	101	0.137	14		
09044.04-MI12 (Fennville, MI/2004)	Zeal® 72WDG	1. Foliar directed air blast/fruiting	102	0.137	-	0.272	None
		2. Foliar directed air blast/fruiting	100	0.135	14		
09044.04-OR16 (Hood River, OR/2004)	Zeal® 72WDG	1. Foliar directed air blast/green, pink and some red fruit	178	0.139	-	0.280	None
		2. Foliar directed air blast/50% ripe fruit	181	0.141	13		
09044.04-WA13 (Prosser, WA/2004)	Zeal® 72WDG	1. Foliar directed air blast/fruiting	147	0.137	-	0.272	None
		2. Foliar directed air blast/fruiting	149	0.135	14		
09044.04-CA112 (Madera, CA/2004)	Zeal® 72WDG	1. Foliar directed air blast/fruiting	131	0.136	-	0.272	None
		2. Foliar directed air blast/80% full fruit color	131	0.135	13		
09044.04-CA113 (Visalia, CA/2004)	Zeal® 72WDG	1. Foliar directed air blast/approx. 1 in. fruit diameter immature fruit	132	0.146	-	0.287	None
		2. Foliar directed air blast/approx. 1 in. fruit diameter immature fruit	125	0.141	13		

[1] EP = End-use Product
[2] GPA = Gallons per acre, L/ha
[3] RTI = Retreatment Interval

TABLE B.1.3. Trial Numbers and Geographical Locations.

EPA Regions	Cherry	
	Submitted	Requested
1	1 (tart)	1 (tart)
5	6 (4 tart and 2 sweet)	6 (4 tart and 2 sweet)
9	1 (tart)	1 (tart)
10	2 (sweet)	2 (sweet)
11	2 (1 tart and 1 sweet)	2 (sweet)
12	1 (sweet)	
Total	13 (7 tart and 6 sweet)	12 (6 tart and 6 sweet)

B.2. Sample Handling and Preparation

Duplicate samples of cherries were harvested at commercial maturity, 6-8 days after treatment (DAT). At the 04-WA13 and 04-MI16 trials, additional cherry samples were harvested at approximately 3, 10, and 14, DAT to determine residue decline. Samples were placed in frozen storage at the test facility within 4 hours. Samples were then shipped by freezer truck to the analytical laboratory at the University of California, Department of Environmental Toxicology, Davis, CA. Upon arrival at the laboratory, samples were assigned sample numbers and stored frozen until sample preparation. Samples were ground with dry ice and returned to frozen storage until extraction for analysis. All samples were stored frozen (ca.-20°C) prior to analysis from collection to analysis for up to 179 days.

B.3. Analytical Methodology

The cherry samples were analyzed for etoxazole using a modification of an analytical method entitled "Determination of V-1283 [2-(2, 6-difluorophenyl)-4-(2-ethoxy-4-tert-butylphenyl)-2-oxazoline] in High Moisture Crops Method RM-37HM, Valent U.S.A. Corporation, Dublin, CA, Date: October 12, 1998." Method RM-37HM has been validated using apples, pears, and strawberries matrices (D283737, J. Tyler, 7/31/2003), and found to be adequate for data collection. A brief description of the methods follows.

Briefly, samples were blended with 20% water/acetone for 5 minutes followed by filtration and concentration. Samples were partitioned with dicloromethane/5% aqueous sodium chloride and cleaned by a tandem Si /carbon solid-phase extraction (SPE) cartridge system. The final extracts were analyzed for etoxazole residues using a GC, coupled to a MSD in a selective-ion monitoring (SIM) mode.

The LOD and LOQ were calculated as 0.0012 and 0.0037 ppm, respectively. The lowest level of method validation (LLMV) in this study was 0.010 ppm etoxazole.

C. RESULTS AND DISCUSSION

In a total of 13 cherry (7 tart and 6 sweet) field trials conducted during 2004, etoxazole was applied as two broadcast foliar applications at approximately 0.135 lb ai/A at a 14-day RTI, for a total of 0.27 lb ai/A/season. Cherries were harvested at commercial maturity, at 6-8 DAT. Additional cherry samples were harvested at 3, 10 and 14, DAT from two trial sites to examine residue decline. A single control and duplicate treated samples were collected from each trial.

The GC/MSD method used to determine etoxazole residues in/on cherry are adequate for data collection. Average method validation recoveries were 95±3%, 95±1%, and 91±2% from cherry samples fortified with etoxazole at 0.01, 0.1 and 1.0 ppm, respectively (Table C.1). Average concurrent method recoveries were 101±2%, 97±5%, 98±1%, and 90±4 from cherry samples fortified with etoxazole at 0.01, 0.1, 0.25, and 0.5 ppm, respectively. Apparent residues of

etoxazole were <LOD in/on all control samples. The validated LOQ is 0.0037 ppm and the LOD was 0.0012 ppm for etoxazole in/on cherries. The LLMV in this study was 0.010 ppm. Adequate sample calculations and chromatograms were provided.

Samples were stored frozen from collection to analysis for up to 179 days (~6 months; Table C.3). In a concurrent storage stability study, cherry samples fortified with 0.10 ppm and analyzed a 193 days had an average recovery of 64% (Table C.2). Additionally, previously-submitted plant storage stability data indicate that etoxazole is stable at -20 °C for at least 3.5 months in apples, 2 months in strawberries, 6 months in orange pulp, 12 months in orange peels, 17 months in cottonseed, 6 months in cotton gin byproducts, 2.3 months in almonds, 6 months in almond hulls, 8.4 months in grapes, 4.5 months in grape juice and 3.5 months in raisins (Memos, J. Tyler, 7/31/03, D283737; and J. Tyler, 3/30/05, D303628). In order to correct for storage dissipation, residue values were corrected.

Detailed residue data from each trial location are reported in Table C.4. A summary of residue data for cherries is presented in Table C.5. The results from the 13 trials indicate that the maximum etoxazole residue in tart and sweet cherries following a total application of etoxazole at approximately 0.27 lb ai/A (PHI = 7 days) were 1.2 ppm and 0.28 ppm, respectively. The results of the decline trials indicate that residues of etoxazole declined to a maximum of 0.25 ppm by 14 days in tart cherries, and 0.096 ppm in sweet cherries.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Etoxazole from Cherry.

Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev (%)
Method Validation Recoveries				
Pitted cherry	0.01	3	98, 95, 93	95±3
	0.1	3	96, 95, 95	95±1
	1.0	3	89, 91, 93	91±2
Concurrent Recoveries				
Pitted cherry	0.01	3	102, 99, 102	101±2
	0.1	5	98, 100, 103, 89, 96	97±5
	0.25	6	99, 9 8, 97, 96, 98, 98	98±1
	0.5	6	94, 84, 89, 90, 93, 93	90±4

TABLE C.2. Summary of Storage Stability Data.

Matrix (RAC)	Spike Level	Interval of Storage Stability (days)	Recoveries (%)	Mean ± std dev (%)
Cherry	0.10	193	60, 63, 68	64±4

TABLE C.3. Summary of Storage Conditions.

Matrix (RAC)	Storage Temperature (°C)	Actual Storage Duration (days)	Interval of Demonstrated Storage Stability (days)
Cherry	<-20	179	193[1]

Storage stability samples fortified with 0.10 ppm and analyzed a 193 days had an average recovery of 64% (Table C.2). Additionally, previously-submitted plant storage stability data indicate that etoxazole is stable at -20 °C for at least 3.5 months in apples, 2 months in strawberries, 6 months in orange pulp, 12 months in orange peels, 17 months in cottonseed, 6 months in cotton gin byproducts, 2.3 months in almonds, 6 months in almond hulls, 8.4 months in grapes, 4.5 months in grape juice and 3.5 months in raisins (Memos, J. Tyler, 7/31/03, D283737; and J. Tyler, 3/30/05, D303628).

TABLE C.4. Residue Data from Crop Field Trials with Etoxazole.

Trial ID (City, State/Year)	EPA Region	Crop/ Variety	Commodity or Matrix	Total Rate (lb a.i./A)	PHI (days)	Residues *[Corrected Residues]*[1] (ppm)	
09044.04-NJ25 (Bridgeton, NJ/2004)	1	Tart Cherry/ North Star	Pitted fruit	0.272	6	0.20 *[0.31]*	0.20 *[0.31]*
09044.04-MI13 (Fennville, MI/2004)	5	Tart Cherry/ Montmorency	Pitted fruit	0.272	7	0.24 *[0.38]*	0.24 *[0.38]*
09044.04-MI14 (Fennville, MI/2004)	5	Tart Cherry/ Montmorency	Pitted fruit	0.279	7	0.26 *[0.41]*	0.21 *[0.33]*
09044.04-MI15 (Fennville, MI/2004)	5	Tart Cherry/ Montmorency	Pitted fruit	0.275	7	0.38 *[0.60]*	0.34 *[0.53]*
09044.04-MI16 (Fennville, MI/2004)	5	Tart Cherry/ Montmorency	Pitted fruit	0.274	3	0.24 *[0.38]*	0.22 *[0.34]*
					7	0.22 *[0.34]*	0.21 *[0.33]*
					10	0.19 *[0.30]*	0.17 *[0.27]*
					14	0.14 *[0.22]*	0.16 *[0.25]*
09044.04-CO11 (Hotchkiss, CO/2004)	9	Tart Cherry/ Montmorency	Pitted fruit	0.277	7	0.34 *[0.53]*	0.31 *[0.48]*
09044.04-ID08 (Buhl, ID/2004)	11	Tart Cherry/ Montmorency	Pitted fruit	0.271	8	0.36 *[0.56]*	0.76 *[1.2]*
09044.04-MI11 (Fennville, MI/2004)	5	Sweet Cherry/ Heidelfingen	Pitted fruit	0.273	7	0.18 *[0.28]*	0.16 *[0.25]*
09044.04-MI12 (Fennville, MI/2004)	5	Sweet Cherry/ Heidelfingen	Pitted fruit	0.272	7	0.089 *[0.14]*	0.12 *[0.19]*
09044.04-OR16 (Hood River, OR/2004)	12	Sweet Cherry/ Bing and Ranier	Pitted fruit	0.280	6	0.17 *[0.27]*	0.14 *[0.22]*
09044.04-WA13 (Prosser, WA/2004)	11	Sweet Cherry/ Brooks	Pitted fruit	0.272	2	0.14 *[0.22]*	0.17 *[0.27]*
					8	0.082 *[0.13]*	0.11 *[0.17]*
					10	0.081 *[0.13]*	0.075 *[0.12]*
					13	0.063 *[0.099]*	0.096 *[0.15]*
09044.04-CA112 (Madera, CA/2004)	10	Sweet Cherry/ Kings	Pitted fruit	0.272	7	0.10 *[0.16]*	0.10 *[0.16]*
09044.04-CA113 (Visalia, CA/2004)	10	Sweet Cherry/ Brooks	Pitted fruit	0.287	8	0.15 *[0.23]*	0.13 *[0.20]*

[1] Residue values were corrected for storage dissipation (64%). Corrected residue values are reported in brackets.

TABLE C.5. Summary of Residue Data from Crop Field Trials with Etoxazole.

Commodity	Total Applic. Rate (lb a.i./A)	PHI (days)	Residue Levels[1] (ppm)					
			N	Min.	Max.	HAFT[2]	Mean	Std. Dev.
Tart Cherry	0.271-0.297	6-8	14	0.31	1.2	0.88	0.48	0.23
Sweet Cherry	0.272-0.287	6-8	12	0.13	0.28	0.29	0.20	0.050

[1] Corrected residue values (see bracketed residues in Table C.4) were used to determine residue summary information.
[2] HAFT = Highest-Average Field Trial.

D. CONCLUSION

The submitted cherry field trial data are adequate and reflect a total of 2 foliar applications of etoxazole (Zeal® 72 WDG) on tart and sweet cherries at a rate of 0.135 lb ai/A/application for a total application rate of 0.27 lb ai/A (PHI= 7 days). The results show that corrected residues of etoxazole (corrected for storage dissipation) in tart and sweet pitted cherries were 0.31-1.2 ppm and 0.13-0.28 ppm, respectively. An acceptable method was used for quantitation of etoxazole residues in/on cherries, and adequate storage stability data are available to support the duration at which the cherry samples were stored frozen from harvest to extraction.

E. REFERENCES

46018505.der.wpd

DP#:	283737
Subject:	Etoxazole. Registration for Use on Cotton, Pome fruits, Strawberries and Imported Oranges. Summary of Analytical Chemistry and Residue Data.
From:	J. Tyler
To:	S. Nguyen/D. Kenny
Date:	4/31/03

DP#:	303628
Subject:	Etoxazole. Registration for Use on Grapes and Tree Nuts, including Pistachios. Summary of Analytical Chemistry and Residue Data. Petition Number 3F6739.
From:	J. Tyler
To:	K. Davis/D. Kenny
Date:	3/30/05

F. DOCUMENT TRACKING

RDI: RAB1 Chemists (08/01/07), G. Kramer (08/15/07).
Petition Number: 6E7150
DP#: 335334
PC Code: 107091

Template Version June 2005.

Etoxazole/107091/IR-4/959857
DACO 7.4.1/7.4.2/OPPTS 860.1500/OECD IIA 6.3.1, 6.3.2, 6.3.3 and IIIA 8.3.1, 8.3.2, 8.3.3 Crop Field Trial/ Residue Decline - Cantaloupe

Primary Evaluator P.V. Shah for Date: 15-AUG-2007
Jennifer R. Tyler, Chemist
Registration Action Branch (RAB1)
Health Effect Division (HED; 7509P)

Approved by Date: 15-AUG-2007
George F. Kramer, Ph.D., Senior Chemist
RAB1/HED (7509P)

STUDY REPORTS:

MRID No. 47003602 R. Leonard (10/20/06) Etoxazole: Magnitude of the Residue on Cantaloupe: Lab Identification Number: 09018.04-VAL01. Study No.: IR-4 PR No. 09018. Unpublished study prepared by IR-4. 191 pages.

EXECUTIVE SUMMARY:

The Interregional Research Project Number 4 (IR-4) has submitted field trial data for etoxazole on cantaloupe. A total of 9 field trials were conducted in the United States during the 2004 growing season encompassing Regions 2 (MD and GA, n=2), 5 (WI, n=1), 6 (TX, n=2), and 10 (NM and CA, n=4).

At each trial location, a total of 2 broadcast foliar applications of Zeal® 72 WDG, a water-dispersible granule formulation containing 72% etoxazole as the active ingredient (ai), were applied at a rate of approximately 0.135 pounds (lb) ai/acre (A)/application at 21-day retreatment intervals (RTIs) for a total application rate of approximately 0.27 lb ai/A. Samples were harvested 5-8 days following the second application. Additional samples were collected at the 04-NM01 at 3, 8, and 14 days after the final application in order to determine residue decline. No additives were added to the spray mixture.

The nitrogen-phosphorus specific flame-ionization detector (NPD) method used to determine etoxazole residues in/on cantaloupe matrices is a slightly modified version of a previously-validated method (Method RM-37). The method was adequately validated in conjunction with the sample analyses. The validated limit of quantitation (LOQ) was 0.0046 ppm and the limit of detection (LOD) was 0.0015 ppm for etoxazole in/on cantaloupe. The maximum frozen storage interval of samples, from harvest to analysis, was 72 days. Storage stability samples fortified with 0.10 ppm and analyzed at 50 and 126 days had average corrected recoveries of 64% and 70%, respectively. Adequate storage stability data are available; however, in order to correct for storage dissipation, residue values were corrected assuming a recovery of 67% at 72 days.

Residues of etoxazole were 0.016-0.12 ppm in/on 18 cantaloupe samples harvested 5-8 days following two foliar applications of etoxazole totaling ~0.27 lb ai/A. The highest-average field

trial residue (HAFT) of etoxazole in cantaloupe was 0.12 ppm.. Residue decline data show that residues of etoxazole decrease in cantaloupe with increasing pre-harvest intervals (PHIs).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document [DP# D334335].

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. There were minor deviations from regulatory requirements; however, none had a negative impact on the validity of the study.

A. BACKGROUND INFORMATION

Etoxazole is a contact acaricide/ovicide primarily used for the control of tetranychid mite species.

TABLE A.1. Test Compound Nomenclature.

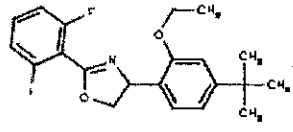
Compound	Chemical Structure
	
Common name	Etoxazole
Company experimental name	S-1283
IUPAC name	(*RS*)-5-*tert*-butyl-2-[2-(2,6-difluorophenyl)-4,5-dihydro-1,3-oxazol-4-yl]phenetole
CAS name	2-(2,6-difluorophenyl)-4-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydrooxazole
CAS #	153233-91-1
End-use product/(EP)	Zeal® 72 WDG

TABLE A.2. Physicochemical Properties.			
Parameter	Value		References
Melting range	101.5-102.5°C		46018505.der.wpd
pH	6.2		
Density	1.2389 g/cm^3		
Water solubility	3.99 x 10^{-5} at 10°C 7.04 x 10^{-5} at 20°C 6.69 x 10^{-5} at 30°C		
Solvent solubility (g/L at 20°C)	acetone: 309 ethyl acetate: 249 methanol: 104	1,2-dichloroethane: 402 n-heptane: 18.7 xylene: 252	
Vapor pressure at 25°C	7.0 x 10^{-6} pascals		
Dissociation constant (pK_a)	no measurable pK_a		
Octanol/water partition coefficient Log(K_{OW})	5.52 ± 0.58 at 20°C		
UV/visible absorption	Not available		

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

TABLE B.1.1 Trial Site Conditions.				
Trial Identification (City, State/Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/g)
09018.04-MD06 (Salisbury, MD/2004)	Loamy sand/Sand (trt2/trt1)	1.1/1.4 (trt2/trt1)	6.0/6.3 (trt2/trt1)	Not reported
09018.04-GA*04 (Tifton, GA/2004)	Loamy sand	0.44	5.9	
09018.04-WI03 (Arlington, WI/2004)	Silt loam	3.6	6.9	
09018.04-TX12 (Weslaco, TX/2004)	Sandy clay loam	0.5	8.0	
09018.04-TX*13 (Weslaco, TX/2004)	Sandy clay	1.1	8.1	
09018.04-NM02 (Mesilla, NM/2004)	Clay loam	0.98	7.89	
09018.04-CA38 (Holtville, CA/2004)	Silty clay loam	0.7	7.8	
09018.04-CA37 (Riverside, CA/2004)	Find sandy loam	0.63/0.58 (trt1/trt2)	7.8/7.9(trt1trt2)	
09018.04-NM01 (Mesilla, NM/2004)	Clay loam	0.98	7.89	

[1] %OM = percent organic matter; CEC = cation-exchange capacity.

Normal weather conditions were reported at all trial sites, with the exception of 04-CA37 and 04-MD06. At the 04-CA37 trial, it was reported that the air temperature was cooler than normal throughout the trial interval. At the 04-MD06 trial, it was reported that the temperature was above normal during May and lower than normal for June and July and that the precipitation was above normal during June and July. The study report noted no unusual conditions that would affect the integrity of the study. Rainfall was supplemented with irrigation as needed.

TABLE B.1.2. Study Use Pattern.

Location (City, State/Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants
		Method/Timing	Volume (GPA[2])	Rate (lb a.i./A)	RTI[3] (days)	Total Rate (lb a.i./A)	
09018.04-MD06 (Salisbury, MD/2004)	Zeal® 72WDG	Foliar broadcast/ 1st small fruits (baseball size)	36.09	0.134	-	0.268	None
		Foliar broadcast/fruit nearly mature	36.16	0.134	21		
09018.04-GA*04 (Tifton, GA/2004)	Zeal® 72WDG	Foliar broadcast/ 3-4 in. avg diameter fruit	32.26	0.136	-	0.274	None
		Foliar broadcast/fruiting	32.68	0.138	20		
09018.04-WI03 (Arlington, WI/2004)	Zeal® 72WDG	Foliar broadcast/fruiting	23.80	0.133	-	0.264	None
		Foliar broadcast/fruiting	23.34	0.131	21		
09018.04-TX12 (Weslaco, TX/2004)	Zeal® 72WDG	Foliar broadcast/ fruit 3-4 in. in diameter	28.18	0.141	-	0.278	None
		Foliar broadcast/ fruit green, fully netted	26.99	0.137	21		
09018.04-TX*13 (Weslaco, TX/2004)	Zeal® 72WDG	Foliar broadcast/fruiting	34.29	0.135	-	0.271	None
		Foliar broadcast/fruiting	32.94	0.136	20		
09018.04-NM02 (Mesilla, NM/2004)	Zeal® 72WDG	Foliar broadcast/ late bloom/early fruit set	55.82	0.137	-	0.273	None
		Foliar broadcast/fruiting	58.27	0.136	22		
09018.04-CA38 (Holtville, CA/2004)	Zeal® 72WDG	Foliar broadcast/ bloom, small fruit	26.18	0.134	-	0.266	None
		Foliar broadcast/ bloom, fruit	23.42	0.132	22		
09018.04-CA37 (Riverside, CA/2004)	Zeal® 72WDG	Foliar broadcast/fruiting	30.14	0.136	-	0.271	None
		Foliar broadcast/ripening fruit	30.00	0.135	22		
09018.04-NM01 (Mesilla, NM/2004)	Zeal® 72WDG	Foliar broadcast/ late bloom, early fruit set	14.38	0.137	-	0.271	None
		Foliar broadcast/fruiting	13.70	0.134	21		

[1] EP = End-use Product
[2] GPA = Gallons per acre, L/ha
[3] RTI = Retreatment Interval

TABLE B.1.3. Trial Numbers and Geographical Locations.

EPA Regions	Cantaloupe	
	Submitted	Requested
2	2	1
5	1	1
6	2	2
10	4	4
Total	9	8

B.2. Sample Handling and Preparation

Duplicate samples of cantaloupe were harvested at commercial maturity, 5-8 days after treatment (DAT). At the 04-NM01 trial, additional cantaloupe samples were harvested at 3, 8, and 14, DAT to determine residue decline. Samples were placed in frozen storage at the test facility within 4 hours. Samples were then shipped by freezer truck to the analytical laboratory at the Valent Technology Center, Valent USA Corporation, Dublin, CA. Upon arrival at the laboratory, samples were assigned sample numbers and stored frozen until sample preparation. Samples were ground with dry ice and returned to frozen storage until extraction for analysis.

All samples were stored frozen (ca.-20°C) prior to analysis from collection to analysis for up to 72 days.

B.3. Analytical Methodology

The cantaloupe samples were analyzed for etoxazole using a modification of an analytical method entitled "Determination of S-1283 in Cottonseed, Method RM-37. Valent U.S.A. Date: June 6, 1997." Method RM-37HM has been validated (D283737, J. Tyler, 7/31/2003), and found to be adequate for data collection. A brief description of the methods follows.

Samples were blended with acetone for 10 minutes then partitioned with dichloromethane/water. The organic phase containing the residues is evaporated and partitioned with acetonitrile/hexane to remove oils. The acetonitrile is then evaporated and the final extracts were analyzed for etoxazole residues using a NPD followed by a silica-gel Sep-Pak.

The LOD and LOQ were calculated as 0.0015 and 0.0046 ppm, respectively. The lowest level of method validation (LLMV) in this study was 0.010 ppm etoxazole.

C. RESULTS AND DISCUSSION

In a total of 9 cantaloupe field trials conducted during 2004, etoxazole was applied as two broadcast foliar applications at approximately 0.135 lb ai/A at a 21-day RTI, for a total of 0.27 lb ai/A/season. Cantaloupe fruit were harvested at commercial maturity, at 5-8 DAT. Additional cantaloupe samples were harvested at 3, 8 and 14, DAT from one trial site to examine residue decline. A single control and duplicate treated samples were collected from each trial.

The NPD method used to determine etoxazole residues in/on cantaloupes are adequate for data collection. Average method validation recoveries were 86±5%, 86±3, and 81±4% from cantaloupe samples fortified with etoxazole at 0.01, 0.1, and 1.0 ppm respectively (Table C.1). Average concurrent method recoveries were 87±6% and 84±6% from cantaloupe samples fortified with etoxazole at 0.01 and 0.1 ppm, respectively. Apparent residues of etoxazole were <LOD in/on all control samples. The validated LOQ is 0.0015 ppm and the LOD was 0.0046 ppm for etoxazole in/on cantaloupes. The LLMV in this study was 0.010 ppm. Adequate sample calculations and chromatograms were provided.

Samples were stored frozen from collection to analysis for up to 72 days (Table C.3). Storage stability samples fortified with 0.10 ppm and analyzed at 50 and 126 days had average corrected recoveries of 64% and 70%, respectively (Table C.2). Additionally, previously-submitted plant storage stability data indicate that etoxazole is stable at -20 °C for at least 3.5 months in apples, 2 months in strawberries, 6 months in orange pulp, 12 months in orange peels, 17 months in cottonseed, 6 months in cotton gin byproducts, 2.3 months in almonds, 6 months in almond hulls, 8.4 months in grapes, 4.5 months in grape juice and 3.5 months in raisins (Memos, J. Tyler, 7/31/03, D283737; and J. Tyler, 3/30/05, D303628). In order to correct for storage dissipation,

residue values were corrected assuming a recovery of 67% at 72 days (average of 64% at 50 days and 70% at 126 days).

Detailed residue data from each trial location are reported in Table C.4. A summary of residue data for cantaloupes is presented in Table C.5. The results from the 9 trials indicate that the maximum etoxazole residue in cantaloupe following a total application of etoxazole at approximately 0.27 lb ai/A (PHI = 5-8 days) was 0.12 ppm. The results of the decline trial indicate that residues of etoxazole declined to a maximum of 0.010 ppm by 14 days.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Etoxazole from Cantaloupe.

Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev (%)
Method Validation Recoveries				
Cantaloupe	0.01	3	82, 91, 84	86±5
	0.1	3	86, 88, 83	86±3
	1.0	3	83, 77, 84	81±4
Concurrent Recoveries				
Cantaloupe	0.01	9	86, 91, 93, 87,77, 95, 85, 88, 78	87±6
	0.1	9	80, 87, 87, 81, 82, 88, 90, 86, 72	84±6

TABLE C.2. Summary of Storage Stability Data.

Matrix (RAC)	Spike Level	Recovery from Fresh Fortified Sample (%)	Interval of Storage Stability (days)	Recoveries (%)	Corrected Mean Recovery (%)[1]
Cantaloupe	0.10	-	0	83, 84, 80	82
		85	50	63, 53, 48	64
		90	126	56, 69, 63	70

[1] Mean recovery of three stored samples divided by the recovery of the freshly fortified sample, multiplied by 100 (except day 0, which is the mean of all three results).

TABLE C.3. Summary of Storage Conditions.

Matrix (RAC)	Storage Temperature (°C)	Actual Storage Duration (days)	Interval of Demonstrated Storage Stability (days)
Cantaloupe	<-20	72	126[1]

Storage stability samples fortified with 0.10 ppm and analyzed a 50 and 126 days had an average corrected recovery of 64 and 70% (Table C.2). Additionally, previously-submitted plant storage stability data indicate that etoxazole is stable at -20 °C for at least 3.5 months in apples, 2 months in strawberries, 6 months in orange pulp, 12 months in orange peels, 17 months in cottonseed, 6 months in cotton gin byproducts, 2.3 months in almonds, 6 months in almond hulls, 8.4 months in grapes, 4.5 months in grape juice and 3.5 months in raisins (Memos, J. Tyler, 7/31/03, D283737; and J. Tyler, 3/30/05, D303628).

TABLE C.4. Residue Data from Crop Field Trials with Etoxazole.

Trial ID (City, State/Year)	EPA Region	Crop/ Variety	Commodity or Matrix	Total Rate (lb a.i./A)	PHI (days)	Residues *[Corrected Recoveries]*[1] (ppm)	
09018.04-MD06 (Salisbury, MD/2004)	2	Cantaloupe/ Athena	Fruit	0.268	7	0.044 *[0.066]*	0.046 *[0.069]*
09018.04-GA*04 (Tifton, GA/2004)	2	Cantaloupe/ Hales Best Jumbo	Fruit	0.274	5	0.022 *[0.033]*	0.020 *[0.030]*
09018.04-WI03 (Arlington, WI/2004)	5	Cantaloupe/ Sweet and Early	Fruit	0.264	8	0.067 *[0.10]*	0.067 *[0.10]*
09018.04-TX12 (Weslaco, TX/2004)	6	Cantaloupe/ Primo	Fruit	0.278	6	0.026 *[0.039]*	0.036 *[0.054]*
09018.04-TX*13 (Weslaco, TX/2004)	6	Cantaloupe/ Cruiser	Fruit	0.271	6	0.027 *[0.040]*	0.044 *[0.066]*
09018.04-NM02 (Mesilla, NM/2004)	10	Cantaloupe/ Topmark	Fruit	0.273	7	0.020 *[0.030]*	0.014 *[0.021]*
09018.04-CA38 (Holtville, CA/2004)	10	Cantaloupe/ Hy-mark	Fruit	0.266	6	0.016 *[0.024]*	0.019 *[0.028]*
09018.04-CA37 (Riverside, CA/2004)	10	Cantaloupe/ Western Sunrise	Fruit	0.271	7	0.080 *[0.12]*	0.079 *[0.12]*
09018.04-NM01 (Mesilla, NM/2004)	10	Cantaloupe/ Topmark	Fruit	0.271	3	0.032 *[0.048]*	0.036 *[0.054]*
					8	0.015 *[0.022]*	0.011 *[0.016]*
					14	0.007 *[0.010]*	0.005 *[0.007]*

[1] Residue values were corrected for storage dissipation (average of 67%). Corrected residue values are reported in brackets.

TABLE C.5. Summary of Residue Data from Crop Field Trials with Etoxazole.

Commodity	Total Applic. Rate (lb a.i./A)	PHI (days)	Residue Levels[1] (ppm)					
			n	Min.	Max.	HAFT[2]	Mean	Std. Dev.
Cantaloupe fruit	0.264-0.278	5-8	18	0.016	0.12	0.12	0.042	0.027

[1] Corrected residue values (see bracketed residues in Table C.4) were used to determine residue summary information.
[2] HAFT = Highest-Average Field Trial.

D. CONCLUSION

The submitted cantaloupe field trial data are adequate and reflect a total of 2 foliar applications of etoxazole (Zeal® 72 WDG) on cantaloupes at a rate of 0.135 lb ai/A/application for a total application rate of 0.27 lb ai/A (PHI= 5-8 days). The results show that residues of etoxazole (corrected for storage dissipation) in cantaloupe were 0.016-0.12 ppm. An acceptable method was used for quantitation of etoxazole residues in/on cantaloupes, and adequate storage stability data are available to support the duration at which the cantaloupe samples were stored frozen from harvest to extraction.

E. REFERENCES

46018505.der.wpd

DP#: 283737
Subject: Etoxazole. Registration for Use on Cotton, Pome fruits, Strawberries and Imported Oranges. Summary of Analytical Chemistry and Residue Data.
From: J. Tyler
To: S. Nguyen/D. Kenny
Date: 4/31/03

DP#: 303628
Subject: Etoxazole. Registration for Use on Grapes and Tree Nuts, including Pistachios. Summary of Analytical Chemistry and Residue Data. Petition Number 3F6739.
From: J. Tyler
To: K. Davis/D. Kenny
Date: 3/30/05

F. DOCUMENT TRACKING

RDI: RAB1 Chemists (3/14/07), G. Kramer (8/15/07).
Petition Number: 6E7150
DP#: 335334
PC Code: 107091

Template Version June 2005.

Etoxazole/107091/IR-4/959857
DACO 7.4.1/7.4.2/OPPTS 860.1500/OECD IIA 6.3.1, 6.3.2, 6.3.3 and IIIA 8.3.1, 8.3.2, 8.3.3 Crop Field Trial/ Residue Decline - Hops

Primary Evaluator P.V. Shah for Date: 15-AUG-2007
Jennifer R. Tyler, Chemist
Registration Action Branch (RAB1)
Health Effect Division (HED; 7509P)

Approved by Date: 15-AUG-2007
George F. Kramer, Ph.D., Senior Chemist
RAB1/HED (7509P)

STUDY REPORTS:

MRID No. 47003603 J. Kowalsky (3/22/06) IR-4 Minor Use Submission in Support of a Tolerance for Etoxazole in or on Hops: Lab Identification Number: 25961. Study No.: IR-4 PR No. 08873. Unpublished study prepared by Valent U.S.A. Corporation. 108 pages.

EXECUTIVE SUMMARY:

The Interregional Research Project Number 4 (IR-4) has submitted field trial data for etoxazole on hops. A total of three field trials were conducted in the United States during the 2003 growing season encompassing Regions 11 (WA and ID, n=2), and 12 (OR, n=1).

At each trial location, a total of 2 foliar airblast applications of Zeal™ 72 WDG, a water-dispersible granule formulation containing 72% etoxazole as the active ingredient (ai), were applied at a rate of approximately 90.7 grams (g) ai/acre (A)/application, for at total application rate of approximately 181.4 g ai/A. For one trial, a second plot was treated with 2 foliar airblast applications at 181.4 g ai/A/application, for a total application rate of 362.8 g ai/A. All applications were made at 14- to 15-day retreatment intervals (RTIs), and hop cones were harvested at commercial maturity, 6-7 days after treatment (DAT). Additional hop samples were harvested at 2, 6, 13, and 20 DAT from one trial site to examine residue decline. All samples were dried in commercial driers after harvest. A single control and duplicate treated samples were collected from each trial.

The gas chromatography (GC) with nitrogen-phosphorus detector (NPD) method used to determine etoxazole residues in/on hop matrices is a modified version of a previously-validated method (Method RM-37). The method was adequately validated in conjunction with the sample analyses. The validated limit of quantitation (LOQ) was 0.2 ppm and the limit of detection (LOD) was 0.1 ppm for etoxazole in/on dried hop cones. The maximum frozen storage interval of samples, from harvest to analysis, was 60 days. Adequate storage stability data are available. Storage stability samples fortified with 0.10 ppm and analyzed at 84 days had an average corrected recovery of 101%.

Residues of etoxazole were 1.98-4.18 ppm in/on 6 dried hop cone samples harvested 6-7 days following two foliar applications of etoxazole totaling ~181.4 g ai/A. The highest-average field

trial (HAFT) residue of etoxazole in dried hop cones was 4.14 ppm. Residue decline data show that residues of etoxazole do not decrease significantly in dried hop cones with increasing pre-harvest intervals (PHIs).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document [DP# 334335].

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. The following deviations from regulatory requirements were reported:

1) For trial V-25961-A, the weather and grower data were not documented in compliance with GLP guidelines.
2) For trial V-25961-B, the crop maintenance activities, including cultivation, maintenance, irrigation, pesticide history records, weather data, grower training records and plot slope were not documented in accordance with GLP guidelines.
3) For trial V-25961-C, the sample weights, meteorological records, soil characteristics, maintenance equipment, fertilizers, pesticides, and pesticide and fertilizer history were not documented in accordance with GLP guidelines.

However, none had a negative impact on the validity of the study.

A. BACKGROUND INFORMATION

Etoxazole is a contact acaricide/ovicide primarily used for the control of tetranychid mite species.

TABLE A.1. Test Compound Nomenclature.	
Compound	Chemical Structure
Common name	Etoxazole
Company experimental name	S-1283
IUPAC name	(*RS*)-5-*tert*-butyl-2-[2-(2,6-difluorophenyl)-4,5-Dihydro-1,3-oxazol-4-yl]phenetole
CAS name	2-(2,6-difluorophenyl)-4-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydrooxazole
CAS #	153233-91-1
End-use product/(EP)	Zeal® 72 WDG

TABLE A.2. Physicochemical Properties.			
Parameter	Value		References
Melting range	101.5-102.5°C		46018505.der.wpd
pH	6.2		
Density	1.2389 g/cm^3		
Water solubility	3.99 x 10^{-5} at 10°C 7.04 x 10^{-5} at 20°C 6.69 x 10^{-5} at 30°C		
Solvent solubility (g/L at 20°C)	acetone: 309 ethyl acetate: 249 methanol: 104	1,2-dichloroethane: 402 n-heptane: 18.7 xylene: 252	
Vapor pressure at 25°C	7.0 x 10^{-6} pascals		
Dissociation constant (pK_a)	no measurable pK_a		
Octanol/water partition coefficient Log(K_{OW})	5.52 ± 0.58 at 20°C		
UV/visible absorption	no ionization at acid or basic pH		

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

TABLE B.1.1 Trial Site Conditions.				
Trial Identification (City, State/Year)	Soil characteristics[1]			
	Type	%OM	pH	CEC (meq/g)
V-25961-A (Zillah,WA/2003)	Not reported			
V-25961-B (Greenleaf, ID/2003)				
V-25961-C (Woodburn, OR/2003)				

[1] %OM = percent organic matter; CEC = cation-exchange capacity.

The study reported noted no unusual conditions that would affect the integrity of the study. Rainfall was supplemented with irrigation as needed.

TABLE B.1.2. Study Use Pattern.

Location (City, State/Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants (%v/v)
		Method/Timing	Volume[2]	Rate (g ai/A)	RTI[3] (days)	Total Rate (g ai/A)	
V-25961-A (Zillah,WA/2003)	Zeal® 72WDG	Foliar airblast/immature	94.7	85.9	-	173.2	Silicon surfactant (0.1%)
		Foliar airblast/immature	96.2	87.3	15		
V-25961-B (Greenleaf, ID/2003)	Zeal® 72WDG	Foliar airblast/hop cones average 1 ¾ inches long	98.5	89.4	-	181.4	Silicon surfactant (0.1%)
		Foliar airblast/near maturity, hop cones to 2 in. long	101.4	92.0	15		
		Foliar airblast/ hop cones average 1 ¾ inches long	99.3	180.2	-	361.7	Silicon surfactant (0.01%)
		Foliar airblast/ near maturity, hop cones to 2 in. long	100.0	181.5	15		
V-25961-C (Woodburn, OR/2003)	Zeal® 72WDG	Foliar airblast/21 days prior to harvest	93.5	83.1	-	165.7	
		Foliar airblast/to 1.5 inch long cones	92.9	82.6	14		

[1] EP = End-use Product.
[2] GPA = Gallons per acre, L/ha.
[3] RTI = Retreatment Interval.

TABLE B.1.3. Trial Numbers and Geographical Locations.		
EPA Regions	Cherry	
	Submitted	Requested
11	2	
12	1	
Total	3	3[1]

[1] A total of 3 trials are requested, but no regions are specified.

B.2. Sample Handling and Preparation

Duplicate samples of hops were harvested at commercial maturity, 6-7 DAT, and dried in commercial driers. At the V-25961-C trial, additional hop samples were harvested at 2, 6, 13 and 20 DAT to determine residue decline. Samples were then shipped by freezer truck to the analytical laboratory at the Valent Technology Center, Valent USA Corporation, Dublin, CA.

Upon arrival at the laboratory, all samples were stored frozen (ca.-20°C) prior to analysis from collection to analysis for up to 60 days. Samples were ground with dry ice prior to analysis.

B.3. Analytical Methodology

Dried hop cone samples were analyzed for etoxazole using a modification of Method RM-37, which has been validated on several commodities (Memo, J. Tyler, 7/31/03; D283737), and found to be adequate for data collection. A brief description of the methods follows.

Briefly, etoxazole residues are extracted from dried hop cone samples with acetone, filtered, and concentrated. The samples are purified using a silica-gel cleanup column, and analyzed by GC using a NPD. The LOD and LOQ were calculated as 0.1 and 0.2 ppm, respectively.

C. RESULTS AND DISCUSSION

In a total of 3 hop field trials conducted during 2003, etoxazole was applied as two foliar airblast applications at approximately 90.7 g ai/A, for a total of 181.4 g ai/A/season. For one trial, a second plot was treated with two foliar airblast applications at 181.4 g ai/A/application, for a total application rate of 362.8 g ai/A. All applications were made at 14- to 15-day RTIs, and hop cones were harvested at commercial maturity, at 6-7 DAT. Additional hop samples were harvested at 2, 6, 13, and 20 DAT from one trial site to examine residue decline. All samples were dried using a commercial drier after harvest. A single control and duplicate treated samples were collected from each trial.

The revised version of Method RM-37 used to determine etoxazole residues in/on hops are adequate for data collection. Average corrected concurrent method recoveries were 99±16% from hop samples fortified with etoxazole at 0.2, 1.0, 2.0 and 5.0 ppm (Table C.1). Apparent residues of etoxazole were <LOD in/on all control samples. The validated LOQ is 0.2 ppm and the LOD was 0.1 ppm for etoxazole in/on hops. Adequate sample calculations and chromatograms were provided.

Samples were stored frozen from collection to analysis for up to 60 days (~2 months; Table C.3). Storage stability samples fortified with 0.10 ppm and analyzed at 84 days had an average corrected recovery of 101% (Table C.2). Additionally, previously-submitted plant storage stability data indicate that etoxazole is stable at -20°C for at least 3.5 months in apples, 2 months in strawberries, 6 months in orange pulp, 12 months in orange peels, 17 months in cottonseed, 6 months in cotton gin byproducts, 2.3 months in almonds, 6 months in almond hulls, 8.4 months in grapes, 4.5 months in grape juice and 3.5 months in raisins (Memos, J. Tyler, 7/31/03, D283737; and J. Tyler, 3/30/05, D303628).

Detailed residue data from each trial location are reported in Table C.4. A summary of residue data for hops is presented in Table C.5. The results from the 3 trials indicate that the maximum etoxazole residue in dried hop cones following a total application of etoxazole at approximately

181.4 g ai/A (PHI = 6-7 days) was 4.18 ppm. The results of the decline trial indicate that residues of etoxazole do not decline significantly over the period tested (0-20 days).

TABLE C.1. Summary of Concurrent Recoveries of Etoxazole from Hops.

Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev (%)
Etoxazole				
Dried hop cones	0.2	3	71, 104, 104	99±15.9
	1.0	3	77, 109, 107	
	2.0	1	110	
	5.0	1	111	

TABLE C.2. Summary of Storage Stability Data.

Matrix (RAC)	Spike Level	Recovery from Fresh Fortified Sample (%)	Interval of Storage Stability (days)	Recoveries (%)	Corrected Mean Recovery (%)[1]
Dried hop cones	1.0	90	0	102, 94	95
		88	84	89, 89	101

[1] Mean recovery of three stored samples divided by the recovery of the freshly fortified sample, multiplied by 100 (except day 0, which is the mean of all three results).

TABLE C.3. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (days)	Interval of Demonstrated Storage Stability (days)
Dried hop cones	<-20	60	84[1]

Storage stability samples fortified with 0.10 ppm and analyzed at 84 days had an average corrected recovery of 101% (Table C.2). Additionally, previously-submitted plant storage stability data indicate that etoxazole is stable at -20 °C for at least 3.5 months in apples, 2 months in strawberries, 6 months in orange pulp, 12 months in orange peels, 17 months in cottonseed, 6 months in cotton gin byproducts, 2.3 months in almonds, 6 months in almond hulls, 8.4 months in grapes, 4.5 months in grape juice and 3.5 months in raisins (Memos, J. Tyler, 7/31/03, D283737; and J. Tyler, 3/30/05, D303628).

TABLE C.4. Residue Data from Crop Field Trials with Etoxazole.

Trial ID (City, State/Year)	EPA Region	Crop/ Variety	Commodity or Matrix	Total Rate (g ai/A)	PHI (days)	Residues (ppm)	
V-25961-A (Zillah,WA/2003)	11	Hop/Warrior	Dried cone	173.2	6	1.98	2.52
V-25961-B (Greenleaf, ID/2003)	11	Hop/Galena	Dried cone	181.4	7	4.18	3.73
				361.7	7	12.84	12.81
V-25961-C (Woodburn, OR/2003)	12	Hop/Liberty	Dried cone	165.7	2	4.98	4.21
					6	4.11	4.17
					13	3.70	3.53
					20	4.28	4.26

TABLE C.5. Summary of Residue Data from Crop Field Trials with Etoxazole.

Commodity	Total Applic. Rate (g ai/A)	PHI (days)	Residue Levels (ppm)					
			N	Min.	Max.	HAFT*	Mean	Std. Dev.
Dried hop cone	165.7-181.4	6-7	6	1.98	4.18	4.14	3.45	0.96

* HAFT = Highest-Average Field Trial.

D. CONCLUSION

The submitted hop field trial data are adequate and reflect a total of 2 foliar applications of etoxazole (Zeal® 72 WDG) on hops at a rate of 90.7 g ai/A/application for a total application rate of 181.4 g ai/A (PHI= 6-7 days). The results show that residues of etoxazole in dried hop cones were 1.98-4.18 ppm. An acceptable method was used for quantitation of etoxazole residues in/on hops, and adequate storage stability data are available to support the duration at which the dried hop cone samples were stored frozen from harvest to extraction.

E. REFERENCES

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DP#:	283737
Subject:	Etoxazole. Registration for Use on Cotton, Pome fruits, Strawberries and Imported Oranges. Summary of Analytical Chemistry and Residue Data.
From:	J. Tyler
To:	S. Nguyen/D. Kenny
Date:	4/31/03

DP#:	303628
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From:	J. Tyler
To:	K. Davis/D. Kenny
Date:	3/30/05

F. DOCUMENT TRACKING

RDI: RAB1 Chemists (8/01/07), G. Kramer (8/15/07).
Petition Number: 6E7150
DP#: 335334
PC Code: 107091

Template Version June 2005.

13544

R151941

Chemical: Triforine

PC Code:
107901
HED File Code: 11000 Chemistry Reviews
Memo Date: 8/15/2007
File ID: *DPD335334*
Accession #: 000-00-0121

HED Records Reference Center
8/31/2007